

REMARKS

Applicants claims stand rejected under 35 U.S.C. §102 in view of Cheng et al. and under 35 U.S.C. §103 in view of various references, i.e., the combination of Lee et al. and Perry et al., the combination of Lee et al. and Chaput et al., the combination of Lee et al. and Piomelli et al. or Liu et al. alone. Applicants disagree as set forth in their response of January 22, 2008 and further in view of the remarks below addressing the rejections under 35 U.S.C. §103.

Applicants have discovered that a ditherapy of metformin and fenofibrate unexpectedly produce synergistic effects. For example, Tables 2 and 3 demonstrate that the combination of metformin and fenofibrate produce effects that are more than the sum of their individual parts.

Table 2, spanning pages 4-5, demonstrates the effects of metformin and fenofibrate on triglyceride levels when administered alone and their synergistic effects when administered in combination. As discussed in paragraphs [0067]-[0069] of the published application. Metformin administered alone did not reduce the triglyceride level as compared to vehicle alone whereas fenofibrate alone significantly reduced the triglyceride levels. Furthermore, combining metformin with fenofibrate resulted in a further reduction of the triglyceride levels over that induced by fenofibrate alone. Such results are unexpected in view of the failure of metformin alone to reduce triglyceride levels.

Table 3, page 5, demonstrates the effects of metformin and fenofibrate on body weight gain when these compounds are administered alone and their synergistic effects when they are administered in combination. In Table 3, the weight variations of the Zucker rats are indicated with individual variations. The differences with the control group were then calculated as mean values with the same calculation method for each treatment. As discussed in paragraph [0081] statistical analysis was carried out using global covariance analysis followed by

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Dunnett's test and that analysis demonstrated that the results obtained were statistically significant. In addition, the simple addition of the percent of body weight reduction achieved by treatments with fenofibrate alone or metformin alone is 31% (26% +5%), whereas their effect on body weight reduction when they are co-administered is 37%, thus demonstrating the synergistic effect achieved by their combination. Unlike In re Kerkhoven 205 U.S.P.Q. 1069 (CCPA 1980) cited by the Examiner, Applicants invention is not a mere mixing of two compounds. Rather, Applicants have demonstrated that the claimed method produces unexpected results and is therefore non-obvious over the cited references.

The cited references and their combinations, i.e., Lee et al. with Perry et al., Lee et al. with Chaput et al., Lee et al. with Piomelli et al., or Liu et al. alone, all fail to teach or suggest the combination of metformin with the particular PPAR α agonist recited in the pending claims, and fail to teach or suggest that these particular combinations would result in a synergistic effect. Thus the references alone or in combination do not render the pending claims obvious.

In view of Applicants previous remarks and these supplemental remarks, Applicants request that the Examiner reconsider and withdraw the rejection of the claims.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and

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please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket #102717.58257US).

Respectfully submitted,

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